

What is Claimed:

1. A method of identifying an individual at an
5 increased risk of breast carcinoma associated with a
polymorphism in a gene, comprising determining the MHC
genotype of an individual and identifying polymorphisms
associated with the predisposition or susceptibility to
breast carcinoma.
- 10 2. The method of claim 1 wherein the polymorphism is
on the TNF- α gene at the -308 locus.
3. The method of claim 1 wherein the polymorphism is
15 on the HSP70-2 gene at the 1267 locus.
4. A method of identifying a predisposition or
susceptibility to breast carcinoma, the method comprising
determining whether the individual possesses a polymorphic
20 risk version of the TNF- α gene, wherein the risk version
has an A at site at the -308 site, the method comprising:
- (a) digestion of corresponding PCR products with the
endonuclease Nco I;
- (b) analysis of amplified fragments by agarose-gel
25 electrophoresis, wherein the presence of Nco I site is
indicated by the cleavage of the 107 bp amplified fragment
to yield fragments of 87 bp and 20 bp, and wherein the two
allelic forms of TNF- α corresponding to the presence or
absence of NcoI are referred to as TNF-1 and TNF-2
30 respectively;
- (c) identifying the presence of susceptibility to
breast carcinomas greatest if that individual is homozygous
for the polymorphic risk version of the gene at the -308
site (TNF2/TNF2).
- 35 5. A method of identifying a predisposition or
susceptibility to breast carcinoma, the method comprising

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determining whether the individual possesses a polymorphic risk version of the HSP70-2 gene, wherein the risk version of the HSP70-2 gene lacks a *Pst* I site at the 1267 position, the method comprising:

- 5 (a) digestion of corresponding PCR products with *Pst* I;
- (b) analysis of amplified fragments by agarose-gel electrophoresis, wherein the presence of the *Pst* I site is indicated by the cleavage of the 2075 bp amplified product
10 to yield fragments of 1139 bp and 936 bp, and wherein the two allelic forms of HSP70-2 gene corresponding to the presence or absence of *Pst* I site are referred to as HSPP1 and HSPP2 respectively;
- (c) identifying the presence of susceptibility to
15 breast carcinomas greatest if that individual is homozygous for the polymorphic risk version of the gene at the 1267 site (P2/P2).

- 20 6. A method of managing and treating patients with a predisposition to breast carcinoma, comprising determining whether the individual possesses a polymorphism in an MHC gene associated with breast carcinoma, wherein the management and treatment of such patient having such polymorphism are promptly treated and managed as patients
25 having a predisposition to breast carcinoma.

7. The method of claim 6 wherein the polymorphism is located on the TNF- α gene at the -308 locus.

- 30 8. The method of claim 6 wherein the polymorphism is located on the HSP70-2 gene at the 1267 locus.

9. A method of screening to identify compounds which stimulate or inhibit the synthesis or action of a
35 polymorphism in an MHC gene associated with breast carcinoma, comprising screening compounds with desired polymorphism sites and identifying those compounds which

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act as agonists toward the sites and those compounds which inhibit activity as antagonists.

10. The method of claim 9 wherein the polymorphism
5 site is selected from the group consisting of TNF- α and HSP70-2.

11. A agonist or antagonist identified by the method
of claim 10.

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12. A method of treating patients comprising
identifying a patient with a predisposition to breast
carcinoma by identifying polymorphisms in an MHC gene
associated with breast carcinoma and administering to such
15 patient an effective amount of an antagonist identified in
claim 11 in a pharmaceutically acceptable carrier.

13. A method of predicting the clinical outcome of a
breast carcinoma patient comprising determining whether the
20 individual possesses a TNF2 homozygous genotype of the TNF- α
gene at the -308 locus wherein the TNF-breast carcinoma-
specific overall survival and disease-free survival are
considered to be shortest in patients carrying the TNF2
homozygous genotype.

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14. A method of predicting the clinical outcome of a
breast carcinoma patient comprising determining whether the
individual possesses a HSP70-2 homozygous genotype, wherein
the survival rate is the longest in the group of breast-
30 carcinoma patients carrying the HSP-P2 homozygous genotype.